

Morbidity and Mortality Characteristics of Asian Strain Influenza

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DURING the fall of 1957 acute respiratory disease occurred in epidemic prevalence in the greater Kansas City area. The clinical and epidemiological picture of illnesses was typical of influenza. The majority were influenza-like, characterized by a sudden onset of fever, headache, malaise, sore throat, coryza, cough, and muscular aching. The outbreak was explosive, disseminated rapidly through the population, and caused high attack rates among persons of all ages. The number of deaths, particularly deaths attributed to pneumonia, increased.

The outbreak was first noted in September 1957 in the southwest section of Kansas City, Mo., where an abrupt rise in absenteeism from respiratory disease was reported from Southwest High School. The disease then appeared in other high schools in the city. The daily rate of absenteeism reported from five high schools during the epidemic period varied from 11 to 38 percent. The usual daily absenteeism had been less than 5 percent. Approximately 4 weeks following the high school outbreaks, a

marked rise in absenteeism was reported in the grammar schools. Inquiries made of four elementary schools on October 15 indicated rates of absenteeism ranging from 33 to 67 percent. There was an abnormal incidence of respiratory infections among workers in various industries in Kansas City, with the peak incidence occurring during the middle of October.

Most of the influenza-like illnesses observed during the epidemic period were probably Asian influenza. This assumption was reflected by the results of etiological studies performed on throat washings (or swabs) and on acute and convalescent serums obtained from several groups of patients with influenza-like illnesses. The specimens came from four principal sources: high school students, student nurses seen at the student health service of the University of Kansas Medical Center, patients seen in offices of private physicians, and patients in various Kansas City hospitals.

An influenza virus which was antigenically related to the Asian strain (A2/Japan/305/57) was recovered from 41 of 75 patients (55 percent) by inoculation of throat washings into the amniotic cavity of 12-day-old embryonated eggs. Acute and convalescent serum samples from 18 of 32 patients showed a fourfold or greater rise in hemagglutination-inhibition antibody titers, with the A2/Japan/305/57 strain of virus used as the antigen. Thirty of the 75 patients from whom throat washings were obtained were seen at the student health service where a separate study on influenza was conducted. Twenty-two of them (73 percent) with illnesses diagnosed clinically as influenza

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were shown to have had Asian influenza (T. D. Y. Chin and R. A. Jordan, unpublished data).

In addition, lung tissue specimens were obtained at autopsy from 11 patients who had pneumonia. The Asian strain of influenza virus was recovered from eight patients by inoculation of tissue suspension intra-amniotically into embryonated eggs.

The data presented in this report describe the morbidity and mortality observations made during the epidemic. The morbidity study was made on a group of high school students and their families. The mortality observations were limited to the influenza and pneumonia deaths reported in Kansas City, Mo. The data describing the efficacy of immunization with monovalent vaccine (A2/Japan/305/57) in prevention of influenza-like illness have been reported in a separate publication (1).

Methods of Study

The morbidity studies were carried out on a group of students of Southwest High School and their families. The school is located in an upper middle-class residential neighborhood in the southwest section of Kansas City. It had an enrollment of 2,123 students attending grades 8-12. Morbidity data were obtained from a questionnaire which was designed to determine the extent of the epidemic in the school and the epidemiological characteristics of influenza occurring in the students and all members of their families. The questionnaire requested the usual identifying data, a family roster, names of the schools children were attending, occurrence of influenza-like illness since August 15, 1957, date of onset and duration of illness, a checklist of symptoms referable to the respiratory system, and a history of vaccination against influenza.

Each student was given a questionnaire to be completed by or under supervision of a parent, and was instructed to return only one completed form per family. The questionnaires were distributed by classroom teachers on October 22, about 1 month after the peak of the epidemic in the school; the completed questionnaires were returned on October 24.

A few families indicated in the questionnaires

that influenza-like illness had occurred during the last week of July and the first part of August. Therefore, the rates presented in this paper were based on the influenza-like illnesses reported between July 25 and October 24.

A total of 1,429 forms were returned. After eliminating 45 inadequate or incomplete forms and 29 duplications, the forms completed by 1,355 families formed the basis for the report. The total population was 5,822 persons (an average of 4.3 per family), including 1,577 members (74 percent) of the student body. No information was available about the characteristics of the remaining 26 percent of the students and their families.

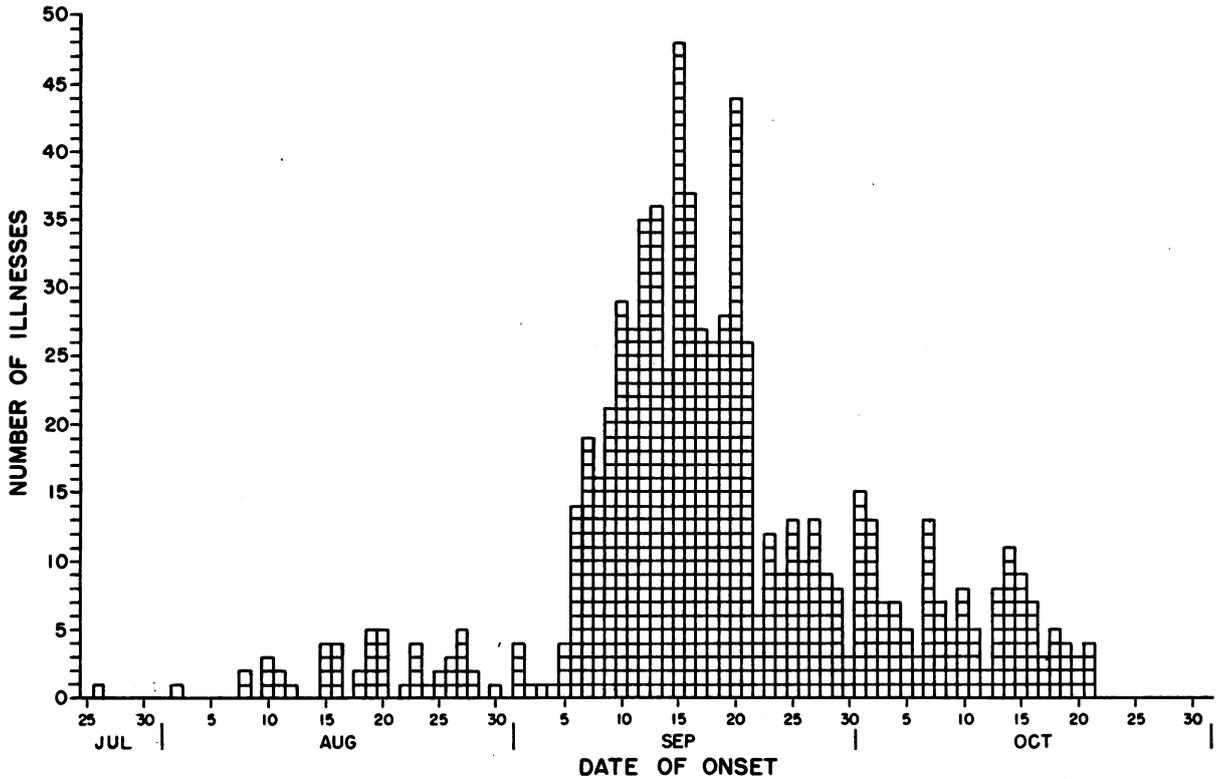
The mortality studies were limited to the reported influenza and pneumonia deaths of residents of Kansas City, Mo., from October 1, 1957, to March 31, 1958. A plan to obtain epidemiological data was organized during the first week of October when a sudden rise in the number of pneumonia deaths was noted. Each week a list of deaths attributed to influenza and pneumonia was obtained from the Kansas City (Mo.) Health Department. For each case epidemiological data were obtained about age, sex, and associations with influenza and with known chronic disease or other conditions, such as pregnancy and postoperative complications. Sources of this information were hospital records and interviews with physicians, relatives, or friends of the deceased. Whenever possible autopsy material consisting of samples of trachea or lung was obtained for virus isolations.

In this study a death was considered related to influenza when one of the following criteria was met: (a) symptoms of influenza were present, (b) influenza-like illness was present concurrently or within 1 week from date of onset of illness in one or more familial associates of the deceased patient, or (c) the Asian strain of influenza virus was recovered from post-mortem tissue specimens.

Morbidity Among Students and Families

The general clinical picture of the illnesses of the students and their families consisted of fever of 100° to 104° F., chills, headache, sore throat, malaise, cough, and coryza. Of the

Figure 1. Incidence of influenza-like illness by date of onset in 745 students of Southwest High School, Kansas City, Mo., 1957



1,927 persons reporting having had an influenza-like illness, 84 percent had fever; 73 percent, headache; 77 percent, cough; 63 percent, sore throat; and 61 percent, coryza. A history of chest pain was given by 23 percent. A majority of the illnesses lasted 3-7 days.

The incidence of influenza-like illness (745 cases with date of onset given) reported among the high school students according to date of onset is depicted in figure 1. During August and the first few days of September, there were only sporadic cases. On September 6, the number of cases increased suddenly. The high attack rates were sustained for the next 2 weeks, and then abruptly declined. Although abnormal incidence continued for 3 additional weeks, the number of cases reported were of a much lower order of magnitude.

The epidemic curve describing the occurrence of 776 cases among the family contacts for which a date of onset was given (fig. 2) is similar to that of the high school students except that the ascending limb was less abrupt and the

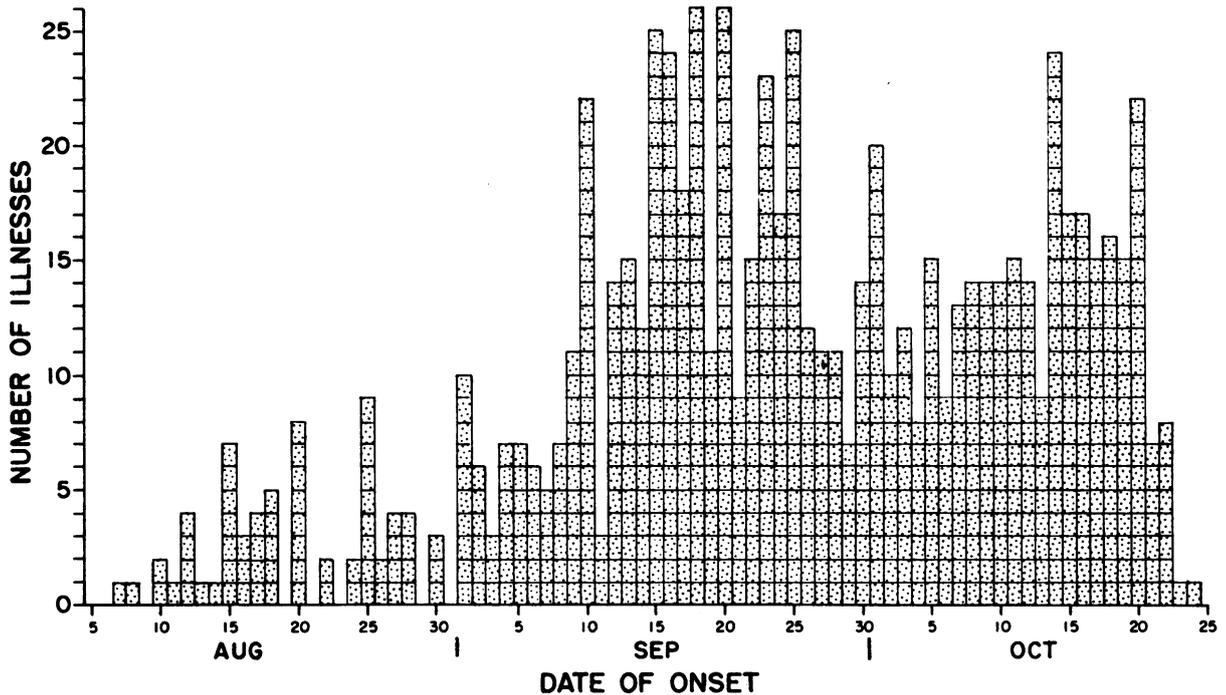
peak of the curve was broader. While the incidence in the high school had fallen precipitously by September 21, incidence continued to be high among the family contacts and was sustained until October 20, after which it abruptly declined.

Thirty-four percent of the 5,822 persons had influenza-like illnesses. The highest attack rate, slightly more than 50 percent, was observed in children aged 10-19 years (table 1 and fig. 3). Among children under 10 years of age, about one-third experienced clinical infection. About 27 percent of the young adults gave a history of having had an influenza-like illness, while in persons 40 years and older the incidence was 17 percent. There was no significant difference in the sex distribution.

The age-specific attack rates among the students attending Southwest High School were relatively uniform, ranging from 50 to 69 percent. The overall attack rate in this group was 59 percent.

The incidence of influenza-like illnesses

Figure 2. Incidence of influenza-like illness by date of onset in 776 family contacts of Southwest High School students, Kansas City, Mo., 1957



among the family contacts of the students of Southwest High School is summarized in table 2. The overall attack rate was 24 percent. The attack rates among children under 20 years of age were relatively uniform, ranging from 32 to 39 percent and decreasing with age. The rates among the teenage family contacts were considerably lower than those observed in the high school students.

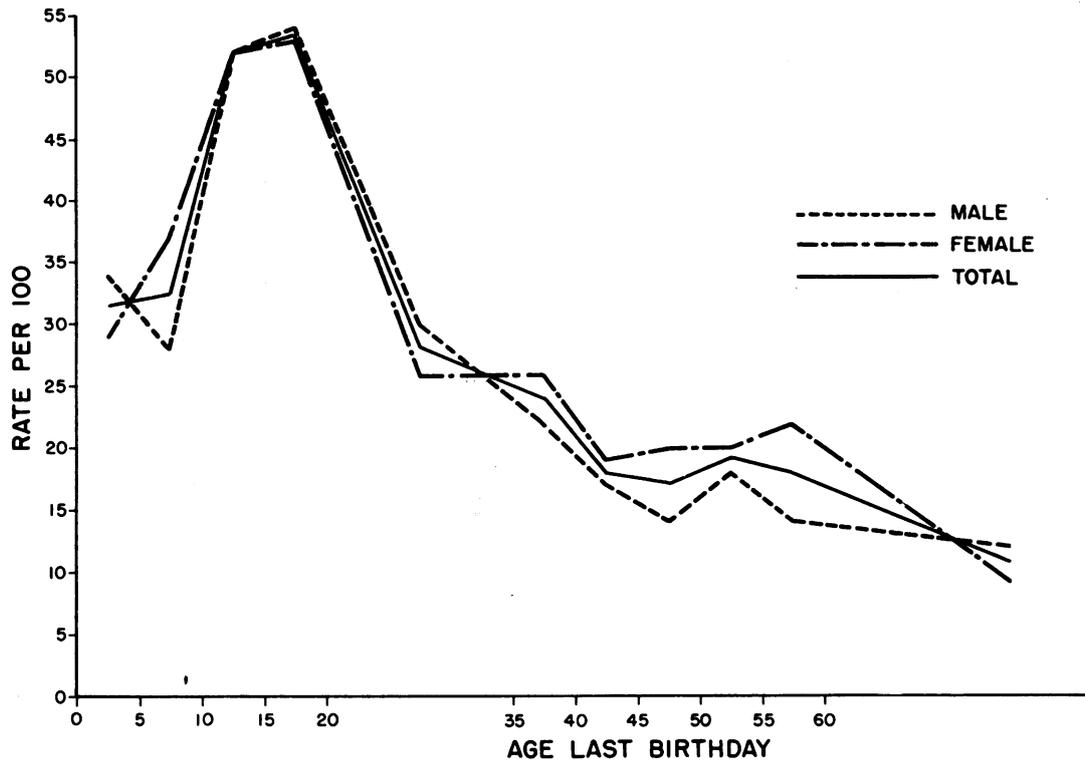
The attack rates with respect to family size are shown in table 3. Of 1,303 families included in this analysis, 85 percent were families with three to five members; the remaining 15 percent had six or more persons per family. The attack rate in three-member households was 30.7 percent; the incidence then gradually increased with family size to 40.5 percent in households having seven or more members per family.

The mean secondary attack rate was 14 percent. This observation was based on 2,596 persons exposed to index cases (first clinical case occurring in a family) in 712 families. The incidence of secondary cases with respect to age is shown in table 4. In calculating these rates, persons who became ill 1-10 days following ex-

posure to index cases were considered secondary cases. As expected, the rates among children were higher than those of adults, with the highest incidence in children aged 10-19 years. The secondary attack rate among children in the age group 10-19 years was slightly higher than that observed in children under 9 years of age; the difference, however, was probably not real, as it could have occurred by chance about 2 out of 10 times ($P=0.23$). The rates among adults in the age groups 20 years and older were substantially lower.

When the distribution of 729 index cases (including 17 co-primary cases) by age was examined, 586 (80 percent) were found to be persons between 10 and 19 years of age. All but nine of these were students attending Southwest High School. As expected, less than 1 percent of the index cases were in children under 5 years. Frequency in age groups 20 years and over ranged from 2 to 4 percent. If index cases were presumed to carry the infection into the household, it appears that in this outbreak the high school students were the most frequent sources of household infections. Unfortu-

Figure 3. Incidence of influenza-like illness by age and sex among 1,355 families, Kansas City, Mo., July 25–October 24, 1957



nately, similar studies were not carried out in an elementary or a junior high school to determine similar relationship.

Influenza and Pneumonia Mortality

The total number of deaths from influenza and pneumonia reported among residents of

Kansas City, Mo., from October 1, 1957, to March 31, 1958, was 253, a mortality rate of 49.6 per 100,000 population for the 6-month period. This incidence is compared with that reported for the same period in each of 5 preceding years (table 5). The rate for the fall and winter, 1952-53, was 35.2, about one-third less than that

Table 1. Incidence of influenza-like illness by age and sex among 1,355 families, Southwest High School, Kansas City, Mo., July 25–October 24, 1957

Age group (years)	Total in survey			Attack rates per 100		
	Male	Female	Total	Male	Female	Total
0-4	76	75	151	34	29	32
5-9	203	221	424	28	37	33
10-14	601	619	1,220	52	52	52
15-19	499	547	1,046	54	53	54
20-34	87	132	219	30	26	27
35-39	130	302	432	22	26	25
40 and over	931	843	1,774	16	19	17
Unknown	210	256	1,556	13	18	17
Total	2,737	2,995	15,822	33	34	34

¹ Includes 90 persons concerning whom information on age and sex was incomplete.

Table 2. Incidence of influenza-like illness among family contacts of students of Southwest High School, Kansas City, Mo., July 25–October 24, 1957

Age group (years)	Number of contacts	Number ill	Attack rate per 100
0-4.....	151	48	32
5-9.....	424	138	33
10-14 ¹	509	198	39
15-19 ¹	181	69	38
20-34.....	219	60	27
35-39.....	432	106	25
40-44.....	737	134	18
45-49.....	535	90	17
50-54.....	280	52	19
55-59.....	101	17	17
60-90.....	119	12	10
Unknown.....	467	73	16
Total.....	4, 155	997	24

¹ High school students in these age groups were attending schools other than Southwest High School.

reported during the 1957–58 epidemic. In the winter of 1952–53 influenza A' infections were prevalent in the United States and were known to cause localized outbreaks in Missouri (2). During the 4 noninfluenza years, the mortality rates were one-half to one-third as high as those observed during the 1957–58 epidemic.

From October 1957 to March 1958, 7.4 per cent of the deaths were attributed to pneumonia and influenza. This figure is significantly higher than that reported for each of the 5 preceding years (table 6). The number of deaths from causes other than pneumonia and influenza was also higher during the 1957–58

Table 3. Incidence of influenza-like illness by size of family, Southwest High School, Kansas City, Mo., July 25–October 24, 1957

Size of family ¹	Number of families	Number of persons	Number ill	Attack rate per 100
3.....	278	834	256	30.7
4.....	539	2, 156	693	32.1
5.....	293	1, 465	490	33.4
6.....	123	738	257	34.8
7, 8, 9, 10.....	70	531	215	40.5
Total.....	1, 303	5, 724	1, 911	33.4

¹ 52 families with 1 and 2 members were not included.

epidemic as compared with that of the 4 non-influenza years.

The number of influenza and pneumonia deaths reported weekly for 1957–58 was compared with the adjusted average for the period 1952–57 (fig. 4). Two distinct waves of excess mortality were observed during the 1957–58 epidemic, one occurring in October and November and the other in the latter part of February. The 1952–57 curve does not show similar rises although the number of deaths increased slightly late in December and in the month of January; the slight increase undoubtedly represents a normal seasonal variation in deaths from acute respiratory disease.

Table 4. Age-specific secondary attack rates of influenza-like illness among family contacts of index cases in 712 families, Southwest High School, Kansas City, Mo., July 25–October 24, 1957

Age last birthday (years)	Total at risk	Number of secondary cases (1-10 days)	Attack rate per 100
0-4.....	83	19	22.9
5-9.....	232	41	17.7
10-14.....	411	89	21.7
15-19.....	309	71	23.0
20-34.....	109	14	12.8
35-39.....	252	37	14.7
40 and over.....	981	82	8.4
Unknown.....	219	15	6.8
Total.....	2, 596	368	14.2

The age-specific mortality rates based on 253 influenza and pneumonia deaths are shown in table 7. The highest rates were observed in the very young and the very old. The rate among children under 1 year was 529 per 100,000 population. In persons 65 years and older the range was from 185 to 521 per 100,000, with the rates rising as age increased. The age-specific death rates for 1957–58 were generally higher than those for the same period in the preceding 5 years. These differences were particularly noticeable in persons under 1 year of age and in the older age groups.

Although the age-specific death rates of the 1957–58 epidemic were higher in certain age groups, the age pattern of influenza and pneu-

Table 5. Pneumonia and influenza deaths reported in Kansas City, Mo., October through March, 1952-58

Year	Number of deaths	Death rate per 100,000 ¹
1952-53.....	165	35. 2
1953-54.....	82	17. 3
1954-55.....	122	25. 4
1955-56.....	87	17. 8
1956-57.....	87	17. 6
1957-58.....	253	49. 6

¹ Based on population estimates, City Health Department, Kansas City, Mo.

monia deaths was essentially unaltered. The age distribution observed in the 1957 epidemic was almost identical to that of the preceding 5 years (fig. 5).

The number of male deaths was significantly higher than female, 147 compared with 106. The probability of this difference occurring by chance is 1 in 100 when the proportion of males to females in the population is assumed to be equal.

Of the 253 influenza and pneumonia deaths, an adequate clinical history was obtained concerning 237. According to the criteria previously defined, 100 of the 237 deaths (42 percent) were associated with influenza; 80 patients had a history of influenza or an influenza-like illness, and 20 did not have symptoms of influenza but influenza-like illnesses were reported among the familial associates. Of the remaining 137 persons, history of influenza was not elicited as a part of the clinical picture nor was influenza observed among their familial associates.

Table 6. Percentage of deaths attributed to pneumonia and influenza, Kansas City, Mo., October through March, 1952-58

Year	Number of deaths from all causes	Number of pneumonia and influenza deaths	Percent of total
1952-53.....	3, 329	165	5. 0
1953-54.....	2, 921	82	2. 8
1954-55.....	2, 919	122	4. 2
1955-56.....	2, 450	87	3. 6
1956-57.....	3, 016	87	2. 9
1957-58.....	3, 439	253	7. 4

Table 7. Influenza and pneumonia death rates by age, Kansas City, Mo., October through March, 1952-57 and 1957-58

Age group (years)	Average, 1952-57		1957-58	
	Number	Rate per 100,000	Number	Rate per 100,000
0-1.....	13	153	45	529
1-4.....	3. 6	11	4	12
5-9.....	. 4	1	3	10
10-14.....	. 8	3	1	4
15-19.....	. 2	1	3	12
20-24.....	. 4	1	3	8
25-29.....	0	0	1	2
30-34.....	. 6	2	0	0
35-39.....	1. 2	3	4	11
40-44.....	. 8	2	10	29
45-49.....	3. 8	12	8	25
50-54.....	3. 8	13	12	40
55-59.....	2. 4	9	15	59
60-64.....	5. 4	25	15	71
65-69.....	6. 8	39	32	185
70-74.....	8	71	26	231
75 and over.....	24	176	71	521
Total.....	75. 2	16	253	56

In 185 deaths (73 percent) there was a history of pre-existing chronic disease or other associated conditions. Fifty percent of the 185 persons had cardiovascular disease, and about 18 percent chronic pulmonary disease. The conditions associated with the 185 deaths are tabulated.

<i>Associated conditions</i>	<i>Number of deaths</i>
Cardiovascular disease.....	92
Chronic pulmonary disease.....	33
Nervous and mental disease.....	15
Diabetes	10
Chronic alcoholism.....	9
Renal disease.....	6
Cancer	5
Rheumatism and allied disease.....	4
Liver disease.....	3
Lower urinary tract infection.....	3
Postoperative complication.....	3
Paget's disease.....	1
Pregnancy	1
Total	185

Discussion

Three main criticisms are immediately evident in this study: (a) the questionnaire method of data collection is not as accurate nor as uniform as data obtained by an experienced medi-

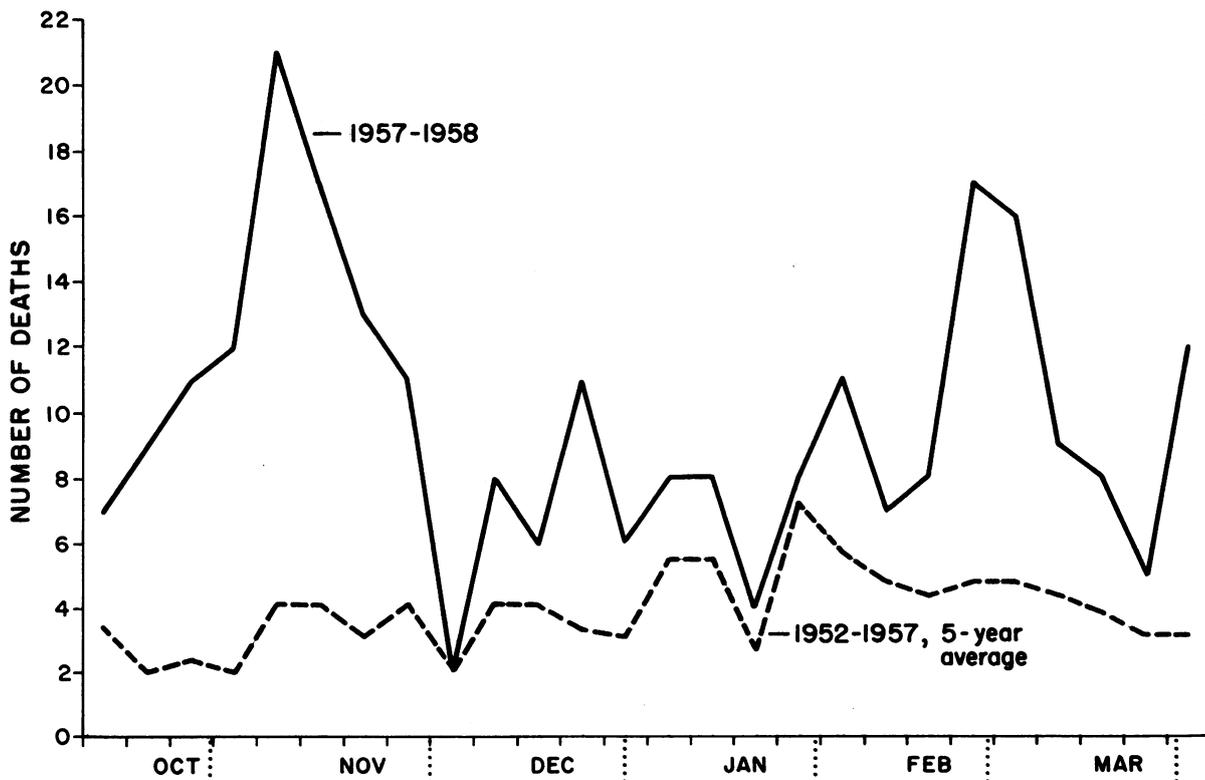
cal interviewer, (b) the population selected was limited to families with children of high school age, and (c) virologic studies were performed on a relatively small sample of cases. Despite these weaknesses, the clinical and epidemiological data derived clearly indicate that the epidemic was influenza and a majority of the illnesses observed during September and October were probably caused by the Asian strain of influenza virus.

The case incidence was high, reflecting the infectiousness of the agent invading a highly susceptible population. The overall morbidity rate of the survey population was 34 percent. The rate among the students attending Southwest High School was considerably higher, however, than that of the teenage household contacts not attending the same school. This observation indicates that the outbreak was cen-

tered in the high school and the infection spread to family contacts. This manner of spread undoubtedly explains the high frequency of index cases observed among the Southwest High School students.

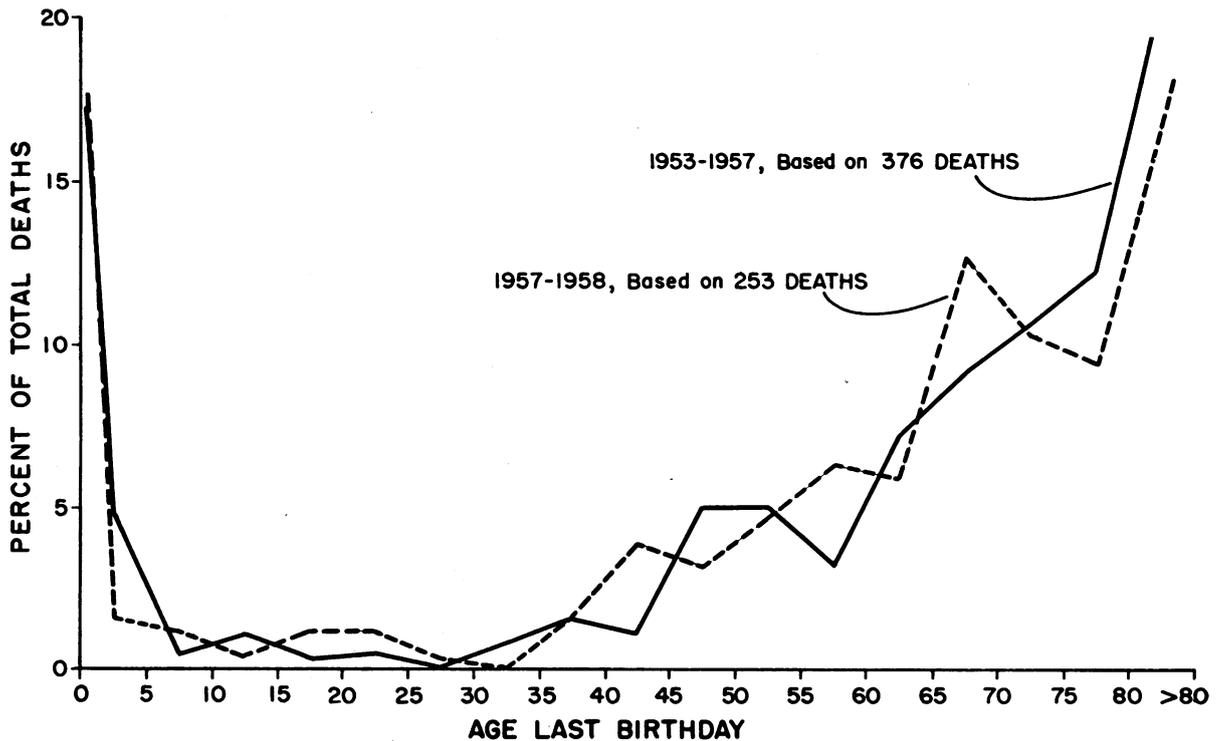
The variations in age-specific incidence are worthy of note. Although the Asian strain showed a marked difference in its antigenic property from all previously known strains of influenza virus and only a small fraction of the older population was shown to possess strain-specific antibody (3,4), not all persons were equally susceptible to the disease. The age distribution curve indicates that susceptibility to Asian influenza was greatest among teenagers, with progressive reduction as age increased. This type of age pattern was also reported in studies of Asian influenza in Louisiana (5) and in Melbourne, Australia (6).

Figure 4. Deaths associated with influenza and pneumonia by week,¹ Kansas City, Mo., October–March, 1957–58 and 1952–57



¹The method of adjustment used to obtain the weekly average for 1952-57 is that described in the 1957 Morbidity and Mortality Weekly Reports published by the National Office of Vital Statistics, Public Health Service.

Figure 5. Percent distribution by age of influenza and pneumonia deaths, Kansas City, Mo., October–March, 1957–58 and 1953–57



The high attack rate observed among teenagers can be partially explained by the increased risk of exposure, since the epidemic was centered in the high school where more than half of the student body had experienced clinical influenza. The progressive decline in the incidence with increasing age probably is a reflection of partial immunity which was presumably acquired as a result of repeated infections with the influenza virus in the past. Evidence in support of this explanation has been suggested by the work of Francis and associates (7, 8) who demonstrated a high degree of correlation between progressive increase in resistance to influenza and acquisition with age of broader antibody spectrum because of repeated experiences with many antigenic variants of influenza virus. The recent study of Hilleman and associates (4) also lends support to this thesis.

Although the attack rate was higher in children aged 10–19 years than in those aged 0–9 years, such age selection was not evident among the family contacts. However, these results

are to be expected when children are exposed in a household environment where the degree of exposure becomes more equal. This observation seems to further support the premise that the increased attack rate which occurred among the teenagers was due to the greater risk of exposure in the school.

Two distinct peaks were clearly evident in the mortality curve, one occurring in the fall of 1957 and the other in February 1958. This pattern is similar to that observed elsewhere in the United States (9). The first wave of excess mortality was coincident with the sharp outbreak of influenza which occurred during the fall. The second, lesser wave of mortality also occurred during a period of increased prevalence of influenza. Infections in the second period were widely scattered and were limited to single families or small groups of persons such as those in hospital wards or in nursing homes. No survey was made to ascertain the extent of influenza occurring in the community at that time. However, examination of the admission records for respiratory disease at the

student health service of the University of Kansas Medical Center clearly indicates that a lesser, second wave of acute respiratory infections occurred in the month of February and the first part of March. Seventeen (90 percent) of 19 patients studied during this secondary wave were etiologically proved to have had Asian influenza (T. D. Y. Chin and R. A. Jordan, unpublished data).

While the number of pneumonia deaths observed in the current epidemic was significantly higher than that reported for the nonepidemic periods, the age pattern of the deaths was essentially unaltered. The skewed U-shaped curve was similar to that seen in Asian influenza outbreaks occurring elsewhere (10,11). There was no indication, however, that it had any resemblance to the pattern of the 1918 experience, when nearly 50 percent of the deaths from influenza and pneumonia were of persons aged 20-40 years (12).

Summary

Asian influenza appeared in epidemic prevalence in the greater Kansas City area during the fall of 1957, followed by a minor secondary wave during the winter of 1958. A survey of 5,822 persons during the fall epidemic revealed an attack rate of 34 percent. The highest attack rate was observed in persons aged 10-19 years, with a decline in rates with increasing age.

The rate of clinical infection was related to family size, varying from 30.7 percent in three-member households to 40.5 percent in households with seven or more members. The secondary attack rate was 14 percent.

A total of 253 deaths due to influenza and pneumonia was reported in Kansas City, Mo., from October 1, 1957, to March 31, 1958, a mortality rate of 49.6 per 100,000. This rate was two to three times higher than that of the 4 preceding noninfluenza years.

Two peaks were observed in the mortality curve, one occurring in October and November, and the secondary peak in the latter part of February. The highest death rates were observed in the very young and the very old.

Seventy-three percent of the persons who died had a history of pre-existing chronic disease or other associated conditions, the majority of which were listed as cardiovascular or chronic pulmonary disease.

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